

# SEQUENCE LISTING

<110> Novo Nordisk A/S

<120> Novel Proteases And Variants Thereof

<130> 5665.204-WO

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<150> PA 1999 01212

<151> 1999-08-31

<150> PA 1999 01500

<151> 1999-10-20

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<170> PatentIn Ver. 2.1

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Ser	Pro	His	Thr	Pro	Val	Ser	Ser	Asp	Pro	Ser	Tyr	Lys	Ala	Glu	Thr	
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Ser	Lys	Ala	Phe	Thr	Gly	Thr	Gly	Lys	Val	Asn	Glu	Thr	Lys	Glu	Lys	
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Sub B1

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Tyr Arg Ala Ile Val His Ile Ser Ser Ser Ile Gly Ser Cys Thr Gly	
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Trp Met Ile Gly Pro Lys Thr Val Ala Thr Ala Gly His Cys Ile Tyr	
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Asp Thr Ser Ser Gly Ser Phe Ala Gly Thr Ala Thr Val Ser Pro Gly	
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Arg Asn Gly Thr Ser Tyr Pro Tyr Gly Ser Val Lys Ser Thr Arg Tyr	
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Phe Ile Pro Ser Gly Trp Arg Ser Gly Asn Thr Asn Tyr Asp Tyr Gly	
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gca atc gaa cta agc gaa ccg atc ggc aat act gtc gga tac ttc gga	624
Ala Ile Glu Leu Ser Glu Pro Ile Gly Asn Thr Val Gly Tyr Phe Gly	
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Tyr Ser Tyr Thr Thr Ser Leu Val Gly Thr Thr Val Thr Ile Ser	
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 Tyr Gly Gly Gln Ser Gly Ser Pro Val Phe Glu Gln Ser Ser Ser Arg  
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Val Leu Ala Gly Thr Val Val Pro Gly Met Asn Asn Ser Gln Trp Ala  
60 65 70  
  
tat ggg cat tat agg gtt act cag att atc tac cct gat caa tac aga 624  
Tyr Gly His Tyr Arg Val Thr Gln Ile Ile Tyr Pro Asp Gln Tyr Arg  
75 80 85  
  
aat aac ggt gct tca gag ttt gat tat gct ata ctt aga gta gca cct 672

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 Tyr Gly His Tyr Arg Val Thr Gln Ile Ile Tyr Pro Asp Gln Tyr Arg  
 75 80 85  
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 90 95 100  
 Asp Ser Asp Gly Arg His Ile Gly Asn Arg Ala Gly Ile Leu Ser Phe  
 105 110 115 120  
 Thr Glu Thr Gly Thr Val Asn Glu Asn Thr Phe Leu Arg Thr Tyr Gly  
 125 130 135  
 Tyr Pro Gly Asp Lys Ile Ser Glu Thr Lys Leu Ile Ser Leu Trp Gly  
 140 145 150  
 Met Val Gly Arg Ser Asp Ala Phe Leu His Arg Asp Leu Leu Phe Tyr  
 155 160 165  
 Asn Met Asp Thr Tyr Phe Gly Gln Ser Gly Ser Pro Val Leu Asn Ser  
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 Val Asp Ser Met Val Ala Val His Asn Ala Gly Tyr Ile Val Gly Gly  
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 Ala Ile Val His Ile Ser Ser Ser Ile Gly Ser Cys Thr Gly Trp Leu  
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 Ile Gly Pro Lys Thr Val Ala Thr Ala Gly His Cys Val Tyr Asp Thr  
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 Pro Ser Gly Trp Gln Ser Gly Asn Ser Asn Tyr Asp Tyr Ala Ala Ile  
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 Glu Leu Ser Gln Pro Ile Gly Asn Thr Val Gly Tyr Phe Gly Tyr Ser  
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 tac acc gct tca tcg ctt gca gga gca ggc gtg acc atc agc gga tat 672  
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Ref-B1

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aat	ttc	aca	agc	tgg	aaa	aac	agc	gca	cag							942	
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Pub 131

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Thr Ser Asp Tyr Asp Met Val Thr Ser Asp Gly Lys Val Ile Ser Ser  
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aca aaa gta gca aat aca aga gtg gca cca tat aat tca att gct tat 336  
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Del B1

Lys	Ile	Leu	Thr	Asn	Gly	His	Cys	Val	Tyr	Asn	Thr	Ala	Ser	Arg	Ser	
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Asn	Leu	Thr	Gly	Thr	Thr	Ile	Lys	Ile	Ser	Gly	Tyr	Pro	Gly	Asp	Lys	
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Val	His	Asn	Ala	Gly	Tyr	Ser	Asn	Gly	Thr	Ile	Asn	Gly	Gly	Pro	Lys	
185					190					195					200	
gca	aca	gct	gcc	ttt	gtt	gaa	ttt	atc	aac	tat	gca	aaa	gca	caa		909
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22-81

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His Thr Pro Val Ser Ser Asp Pro Ser Tyr Lys Pro Asp Ser Ser Ala	
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Ser Tyr Asp Pro Ala Ile Lys Thr Asn Lys Asn Gly Ala Tyr Ser Lys	
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gca ttt gaa ggt aca gga aaa cta gac gct ccc ctt tat cag gaa aaa	240
Ala Phe Glu Gly Thr Gly Lys Leu Asp Ala Pro Leu Tyr Gln Glu Lys	
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Tyr Pro Tyr Arg Ala Ile Val His Ile Ser Ser Ser Ile Gly Ser Cys	
20 25 30	
acc ggc tcc ctg atc ggt ccg aaa acg gtg gca acg gcc gga cac tgc	432
Thr Gly Ser Leu Ile Gly Pro Lys Thr Val Ala Thr Ala Gly His Cys	
35 40 45	
att tat gac aca gcg agc ggg tca ttc gcc gga acc gct acc gtt tct	480
Ile Tyr Asp Thr Ala Ser Gly Ser Phe Ala Gly Thr Ala Thr Val Ser	
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Pro Gly Arg Asn Gly Ser Thr Tyr Pro Tyr Gly Ser Val Thr Ser Thr	
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Tyr Gly Ala Ile Glu Leu Ser Gln Pro Ile Gly Asn Thr Val Gly Tyr	
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ttc gga tat tcc tac acc acc tcc tct ctg gtt ggg tca agc gtt acc	672
Phe Gly Tyr Ser Tyr Thr Thr Ser Ser Leu Val Gly Ser Ser Val Thr	
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Ile Ile Gly Tyr Pro Gly Asp Lys Thr Ser Gly Thr Gln Trp Gln Met	
130 135 140	
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Ser Gly Asn Ile Ala Val Ser Glu Thr Tyr Lys Leu Gln Tyr Ala Ile	
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Asp Thr Tyr Gly Gly Gln Ser Gly Ser Pro Val Tyr Glu Ala Ser Ser	
165 170 175	
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Ser Arg Thr Asn Cys Ser Gly Pro Cys Ser Leu Ala Val His Thr Asn	

151

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But 121

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Asp	Phe	His	Asn	Asp	Met	Lys	Thr	Pro	Ser	Ser	Phe	Asp	Lys	Val	Asp	
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Leu	Lys	Asp	Phe	Gln	Thr	Lys	Val	Val	Ile	Gly	Asp	Asp	Gly	Arg	Thr	
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Lys	Val	Thr	Asn	Thr	Arg	Val	Ala	Pro	Tyr	Asn	Ser	Ile	Ala	Tyr	Ile	
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Thr	Phe	Gly	Gly	Ser	Ser	Cys	Thr	Gly	Thr	Leu	Ile	Ala	Pro	Asn	Lys	
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Ile	Leu	Thr	Asn	Gly	His	Cys	Val	Tyr	Asn	Thr	Ala	Thr	Arg	Ser	Tyr	

Variable	Mean	SD	Min	Max
Age	35.2	12.5	18	65
Gender	50.0	0.0	0	1
Marital status	65.0	15.0	0	100
Education	12.5	2.0	8	16
Income	30.0	10.0	10	50
Health status	70.0	10.0	50	90
Life satisfaction	60.0	15.0	30	90
Stress level	40.0	10.0	20	60
Work-life balance	55.0	12.0	35	75
Family support	60.0	10.0	40	80
Community involvement	45.0	15.0	25	65
Personal growth	50.0	10.0	30	70
Financial stability	55.0	12.0	35	75
Emotional well-being	60.0	10.0	40	80
Physical health	70.0	10.0	50	90
Mental health	65.0	12.0	45	85
Social support	55.0	10.0	35	75
Life goals	60.0	15.0	40	80
Work satisfaction	50.0	10.0	30	70
Family time	45.0	12.0	25	65
Personal time	40.0	10.0	20	60
Community time	35.0	8.0	15	55
Work time	30.0	7.0	10	50
Family support score	60.0	10.0	40	80
Community support score	45.0	15.0	25	65
Personal growth score	50.0	10.0	30	70
Financial stability score	55.0	12.0	35	75
Emotional well-being score	60.0	10.0	40	80
Physical health score	70.0	10.0	50	90
Mental health score	65.0	12.0	45	85
Social support score	55.0	10.0	35	75
Life goals score	60.0	15.0	40	80
Work satisfaction score	50.0	10.0	30	70
Family time score	45.0	12.0	25	65
Personal time score	40.0	10.0	20	60
Community time score	35.0	8.0	15	55
Work time score	30.0	7.0	10	50

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15

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Ile Leu Thr Asn Gly His Cys Val Tyr Asn Thr Ala Thr Arg Ser Tyr  
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Ser Ala Lys Gly Ser Val Tyr Pro Gly Met Asn Asp Ser Thr Ala Val  
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75 80 85  
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Arg Glu Asp Thr Asn Leu Ala Tyr Tyr Thr Ile Asp Thr Phe Ser Gly  
155 160 165  
Asn Ser Gly Ser Ala Met Leu Asp Gln Asn Gln Gln Ile Val Gly Val  
170 175 180 185  
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But 131

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Arg	Ala	Thr	Val	Gln	Leu	Ser	Ile	Lys	Tyr	Pro	Asn	Thr	Ser	Ser	Thr		
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Tyr	Gly	Cys	Thr	Gly	Phe	Leu	Val	Asn	Pro	Asn	Thr	Val	Val	Thr	Ala		
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Leu	Ser	Ser	Ser	Val	Thr	Gly	Phe	Pro	Cys	Asp	Lys	Thr	Phe	Gly	Thr		
				135				140					145				
atg	tgg	tct	gat	aca	aag	ccg	att	cgc	tcc	gct	gaa	acg	tat	aag	ctg	768	
Met	Trp	Ser	Asp	Thr	Lys	Pro	Ile	Arg	Ser	Ala	Glu	Thr	Tyr	Lys	Leu		
		150					155					160					
acc	tat	aca	acc	gat	acg	tac	ggc	tgc	caa	agc	ggc	tcg	cct	gtt	tat	816	
Thr	Tyr	Thr	Thr	Asp	Thr	Tyr	Gly	Cys	Gln	Ser	Gly	Ser	Pro	Val	Tyr		
	165					170					175						
cga	aac	tac	agt	gat	aca	ggg	cag	aca	gct	att	gcc	att	cac	acc	aac	864	
Arg	Asn	Tyr	Ser	Asp	Thr	Gly	Gln	Thr	Ala	Ile	Ala	Ile	His	Thr	Asn		
	180				185					190					195		

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gga gga tcg tca tat aac ttg gga aca agg gtg acg aac gat gta ttc 912  
Gly Gly Ser Ser Tyr Asn Leu Gly Thr Arg Val Thr Asn Asp Val Phe  
200 205 210

aac aat att caa tat tgg gca aat caa 939  
Asn Asn Ile Gln Tyr Trp Ala Asn Gln  
215 220

<210> 14  
<211> 313  
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<213> Bacillus subtilis IS75

<400> 14  
Met Lys Leu Val Pro Arg Phe Arg Lys Gln Trp Phe Ala Tyr Leu Thr  
-90 -85 -80

Val Leu Cys Leu Ala Leu Ala Ala Val Ser Phe Gly Val Pro Ala  
-75 -70 -65

Lys Ala Ala Glu Asn Pro Gln Thr Ser Val Ser Asn Thr Gly Lys Glu  
-60 -55 -50

Ala Asp Ala Thr Lys Asn Gln Thr Ser Lys Ala Asp Gln Val Ser Ala  
-45 -40 -35 -30

Pro Tyr Glu Gly Thr Gly Lys Thr Ser Lys Ser Leu Tyr Gly Gly Gln  
-25 -20 -15

Thr Glu Leu Glu Lys Asn Ile Gln Thr Leu Gln Pro Ser Ser Ile Ile  
-10 -5 -1 1

Gly Thr Asp Glu Arg Thr Arg Ile Ser Ser Thr Thr Ser Phe Pro Tyr  
5 10 15

Arg Ala Thr Val Gln Leu Ser Ile Lys Tyr Pro Asn Thr Ser Ser Thr  
20 25 30 35

Tyr Gly Cys Thr Gly Phe Leu Val Asn Pro Asn Thr Val Val Thr Ala  
40 45 50

Gly His Cys Val Tyr Ser Gln Asp His Gly Trp Ala Ser Thr Ile Thr  
55 60 65

Ala Ala Pro Gly Arg Asn Gly Ser Ser Tyr Pro Tyr Gly Thr Tyr Ser  
70 75 80

Gly Thr Met Phe Tyr Ser Val Lys Gly Trp Thr Glu Ser Lys Asp Thr  
85 90 95

Asn Tyr Asp Tyr Gly Ala Ile Lys Leu Asn Gly Ser Pro Gly Asn Thr  
100 105 110 115

Val Gly Trp Tyr Gly Tyr Arg Thr Thr Asn Ser Ser Ser Pro Val Gly  
120 125 130

Leu Ser Ser Ser Val Thr Gly Phe Pro Cys Asp Lys Thr Phe Gly Thr  
135 140 145

Met Trp Ser Asp Thr Lys Pro Ile Arg Ser Ala Glu Thr Tyr Lys Leu  
150 155 160

Thr Tyr Thr Thr Asp Thr Tyr Gly Cys Gln Ser Gly Ser Pro Val Tyr  
165 170 175

But B1

Arg Asn Tyr Ser Asp Thr Gly Gln Thr Ala Ile Ala Ile His Thr Asn  
180 185 190 195  
Gly Gly Ser Ser Tyr Asn Leu Gly Thr Arg Val Thr Asn Asp Val Phe  
200 205 210  
Asn Asn Ile Gln Tyr Trp Ala Asn Gln  
215 220

<210> 15  
<211> 4  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Variation

<400> 15  
Glu Lys Ala Ser  
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<210> 16  
<211> 6  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Variation

<400> 16  
Ser Glu Lys Ala Ser Thr  
1 5

<210> 17  
<211> 4  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Variation

<400> 17  
Ser Glu Glu Thr  
1

<210> 18  
<211> 38  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Primer

<221> misc\_feature  
<222> (1)...(38)  
<223> n = A,T,C or G

<400> 18  
ggatggagaa gcggaacac naaytaygay tayggngc

<210> 19  
<211> 10

38

over 134

<212> PRT  
<213> Artificial Sequence  
  
<220>  
<223> Variation  
  
<400> 19  
Gly Trp Arg Ser Gly Asn Tyr Asp Tyr Gly  
1 5 10

<210> 20  
<211> 28  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Primer

<221> misc\_feature  
<222> 12,15  
<223> n = deoxyInosine

<221> misc\_feature  
<222> 18,21 24  
<223> n = A,T,C or G

<400> 20  
cccaagcttg tngynacngc nggncayt

28

<210> 21  
<211> 6  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Variation

<221> VARIANT  
<222> 2<223> Xaa = Ala or Val

<400> 21  
Val Xaa Thr Ala Gly His  
1 5

<210> 22  
<211> 36  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Primer

<221> misc\_feature  
<222> (1)...(36)  
<223> n = A,T,C or G

<400> 22  
gaataccggt gaaccgcttt gncmncrta ngtrtc

36

<210> 23  
<211> 12  
<212> PRT  
<213> Artificial Sequence

ket 131  
<220>  
<223> Variation  
  
<221> VARIANT  
<222> 5  
<223> Xaa = Gly or Cys or Trp  
  
<400> 23  
Asp Thr Tyr Gly Xaa Gln Ser Gly Ser Pro Val Phe  
1 5 10

<210> 24  
<211> 26  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Primer

<221> misc\_feature  
<222> (1)...(26)  
<223> n = A,T,C or G

<400> 24  
gctctagagt ydatngcncc rtartc

26

<210> 25  
<211> 6  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Variation

<221> VARIANT  
<222> 6  
<223> Xaa = Glu or Lys

<400> 25  
Asp Tyr Gly Ala Ile Xaa  
1 5

<210> 26  
<211> 143  
<212> DNA  
<213> Bacillus

<400> 26  
gcgtctatga cacggcaagc cgatcattcg cggaacccg caccgtttcc ccgggacgaa  
acggttcagc ttaccottac ggatctgtta catcgacccg ctatttcac ccgtcgggtt  
ggcagagcgg aaattccaat tat

60  
120  
143

<210> 27  
<211> 48  
<212> PRT  
<213> Bacillus

<400> 27  
Cys Val Tyr Asp Thr Ala Ser Arg Ser Phe Ala Gly Thr Ala Thr Val  
1 5 10 15  
Ser Pro Gly Arg Asn Gly Ser Ala Tyr Pro Tyr Gly Ser Val Thr Ser  
20 25 30  
Thr Arg Tyr Phe Ile Pro Ser Gly Trp Gln Ser Gly Asn Ser Asn Tyr  
35 40 45

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<210> 28  
<211> 184  
<212> DNA  
<213> Bacillus

<400> 28  
gatcgagctc agccagccga tcggcaatac cgtcggatat ttccggatatt catacaccgc 60  
ttcatcgctt gcaggagcag gcgtgaccat cagcggatat ccaggagaca aaacaacagg 120  
caccagtggt gaaatgtccg gaacgatcgc tgtttcagaa acgtataaac tgcaatatgc 180  
gatc 184

<210> 29  
<211> 61  
<212> PRT  
<213> Bacillus

<400> 29  
Ile Glu Leu Ser Gln Pro Ile Gly Asn Thr Val Gly Tyr Phe Gly Tyr  
1 5 10 15  
Ser Tyr Thr Ala Ser Ser Leu Ala Gly Ala Gly Val Thr Ile Ser Gly  
20 25 30  
Tyr Pro Gly Asp Lys Thr Thr Gly Thr Gln Trp Gln Met Ser Gly Thr  
35 40 45  
Ile Ala Val Ser Glu Thr Tyr Lys Leu Gln Tyr Ala Ile  
50 55 60

<210> 30  
<211> 143  
<212> DNA  
<213> Bacillus

<400> 30  
gcatttatga cacagcgagc gggtcattcg ccggaaccgc taccgtttct ccgggacgga 60  
acggttcaac atatccgtac ggatcagtta catcaaccgc ctatttcatac ccgtcaggct 120  
atcgaagcgg aaattcgaat tac 143

<210> 31  
<211> 48  
<212> PRT  
<213> Bacillus

<400> 31  
Cys Ile Tyr Asp Thr Ala Ser Gly Ser Phe Ala Gly Thr Ala Thr Val  
1 5 10 15  
Ser Pro Gly Arg Asn Gly Ser Thr Tyr Pro Tyr Gly Ser Val Thr Ser  
20 25 30  
Thr Arg Tyr Phe Ile Pro Ser Gly Tyr Arg Ser Gly Asn Ser Asn Tyr  
35 40 45

<210> 32  
<211> 184  
<212> DNA  
<213> Bacillus

<400> 32  
catagagctc agccagccga tcggcaaacac cgtcgggtat ttccggatatt cctacaccac 60  
ctcgtctctc gttgggtcaa gcgttaccat catcggatat ccaggcgaca aaacatcggg 120  
caccgaatgg cagatgtccg gaaatatcgc cgtctcagaa acatataaac tgcaatatgc 180  
gatc 184

<210> 33  
<211> 61  
<212> PRT  
<213> Bacillus

124 131

<400> 33  
Ile Glu Leu Ser Gln Pro Ile Gly Asn Thr Val Gly Tyr Phe Gly Tyr  
1 5 10 15  
Ser Tyr Thr Thr Ser Ser Leu Val Gly Ser Ser Val Thr Ile Ile Gly  
20 25 30  
Tyr Pro Gly Asp Lys Thr Ser Gly Thr Gln Trp Gln Met Ser Gly Asn  
35 40 45  
Ile Ala Val Ser Glu Thr Tyr Lys Leu Gln Tyr Ala Ile  
50 55 60

<210> 34  
<211> 19  
<212> DNA  
<213> Bacillus

<400> 34  
cgtaagggta agctgaacc 19

<210> 35  
<211> 23  
<212> DNA  
<213> Bacillus

<400> 35  
caggagacaa aacaacagca ggc 23

<210> 36  
<211> 18  
<212> DNA  
<213> Bacillus

<400> 36  
gtccccggaga aacggtag 18

<210> 37  
<211> 20  
<212> DNA  
<213> Bacillus

<400> 37  
caccacctcg tctctcgttg 20

<210> 38  
<211> 29  
<212> DNA  
<213> Bacillus

<220>  
<221> misc\_feature  
<222> 18,21  
<223> Xaa = deoxyInosine

<221> misc\_feature  
<222> 27  
<223> n = A, G, C or T

<400> 38  
gctctagacg tyttrtcncm nggrwancc 29

<210> 39  
<211> 7  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Variation

221> VARIANT  
222> 2  
223> Xaa = is Tyr or Phe

221> VARIANT  
222> 4  
223> Xaa = is Gly or Cys

400> 39  
Gly Xaa Pro Xaa Asp Lys Thr  
1 5

210> 40  
211> 29  
212> DNA  
213> Artificial Sequence

220>  
223> Primer

221> misc\_feature  
222> 12,15,21  
223> n = is deoxyInosine

400> 40  
cccaagcttg tngtnathgg ngaygaygg

29

210> 41  
211> 8  
212> PRT  
213> Artificial Sequence

220>  
223> Variation

400> 41  
Val Val Ile Gly Gly Asp Asp Gly  
1 5

210> 42  
211> 29  
212> DNA  
213> Artificial Sequence

220>  
223> Primer

400> 42  
gcacggaccg ttgcagttcg ttctggagc

29

210> 43<211> 33  
212> DNA  
213> Artificial Sequence

220>  
223> Primer

400> 43  
cgggcaaagt gaatgaaaca aaggaaaaag cgg

33

210> 44  
211> 31  
212> DNA



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<213> Artificial Sequence

<220>

<223> Primer

<221> misc\_feature

<222> (1)..(31)

<223> n = A,T,C or G

<400> 44

atgcaccgga tggnnhatag gtccgaaaac c

31

<210> 45

<211> 21

<212> DNA

<213> Artificial Sequence

<220>

<223> Primer

<400> 45

ccctttaacc gcacaggtt t

21